	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	440	antibiotic adj peptide	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 09:51			0
2	BRS	L2	10	beta$1stranded	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 09:52			0
3	BRS	L3	0	1 same 2	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 09:52			0
4	BRS	L4	14	beta adj stranded	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 09:52			0
5	BRS	L5	0	1 same 4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 09:52			0
6	BRS	L6	484	definsin or protegrin or tachyplesin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 09:53			0
7	BRS	L7	4798	(disulfide adj bond) same reduc$5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 09:56			0
8	BRS	L8	5	7 same (1 or 5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 09:57			0
9	BRS	L9	74	no adj disulfide adj bond	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 09:56			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
10	BRS	L10	0	9 same (1 or 5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 09:57			0
11	BRS	L11	1371726	target$3 or vector$3 or transport$3	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 10:02			0
12	BRS	L12	92	11 same (1 or 6)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 09:59			0
13	BRS	L13	4	12 same (active adj substance)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 10:02			0
14	BRS	L14	805720	peptide or polynucleotide or antibody or molecule	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 10:02			0
15	BRS	L15	85	12 same 14	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 10:03			0
16	BRS	L16	0	12 same (biological adj molecule)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 10:03			0
17	BRS	L17	9	calas adj bernard.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 10:04			0
18	BRS	L18	5	grassy adj gerard.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 10:04			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
19	BRS	L19	3	chavanieu adj alain.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 10:05			0
20	BRS	L20	8	kaczorek adj michel.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 10:05			0
21	BRS	L21	1	(17 or 18 or 19 or 20) and 1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/29 10:06			0

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FILE 'MEDLINE' ENTERED AT 10:08:59 ON 29 MAY 2003

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FILE 'AGRICOLA' ENTERED AT 10:08:59 ON 29 MAY 2003

=> s antibiotic peptide
L1         4249 ANTIBIOTIC PEPTIDE

=> s beta-strand?
L2        13485 BETA-STRAND?

=> s beta strand?
L3        13485 BETA STRAND?

=> s l1 (p) l2
L4            1 L1 (P) L2

=> d l4 1 ibib abs

L4   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2003:319744  CAPLUS
DOCUMENT NUMBER:          138:336406
TITLE:                    Antigen conjugated with .  ***beta***  .-
                            ***stranded***     ***antibiotic***     ***peptide***
                          for enhancing cytotoxic T lymphocyte immune response
INVENTOR(S):              Johnson, Mark Elliott; Hamilton, Day Fiona; Kaczorek,
                          Michel; Temsamani, Jamal
PATENT ASSIGNEE(S):       Synt:em S.A., Fr.
SOURCE:                   PCT Int. Appl., 57 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

      PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
      ---------------   ----  --------       ---------------  --------
      WO 2003033021      A1   20030424       WO 2002-EP11500  20021015
          W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
              GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
              LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
              PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
              UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
              TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
              CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
              PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
              NE, SN, TD, TG
PRIORITY APPLN. INFO.:                    EP 2001-402671   A  20011016
AB   The invention relates to conjugates of an antigen coupled to a linear
     deriv. of a ss-stranded antibiotic peptide, which are useful for
     immunogenic agents to enhance a CTL response.  Two groups of preferred
     peptides are derived from the antibiotics protegrin and tachyplesin.
REFERENCE COUNT:          4     THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
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=> d his

     (FILE 'HOME' ENTERED AT 10:08:38 ON 29 MAY 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     10:08:59 ON 29 MAY 2003
L1          4249 S ANTIBIOTIC PEPTIDE
L2         13485 S BETA-STRAND?
L3         13485 S BETA STRAND?
L4             1 S L1 (P) L2

=> s peptide (P) antibiotic (p) l2
L5            33 PEPTIDE (P) ANTIBIOTIC (P) L2

=> duplicate remove l5
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L5
L6            12 DUPLICATE REMOVE L5 (21 DUPLICATES REMOVED)

=> s l6 not l4
L7            11 L6 NOT L4

=> d l7 1-11 ibib abs

L7   ANSWER 1 OF 11     MEDLINE
ACCESSION NUMBER:   2002733905     MEDLINE
DOCUMENT NUMBER:    22384364   PubMed ID: 12399464
TITLE:              Correlations of cationic charges with salt sensitivity and
                    microbial specificity of cystine-stabilized beta -strand
                    antimicrobial peptides.
AUTHOR:             Tam James P; Lu Yi-An; Yang Jin-Long
CORPORATE SOURCE:   Department of Microbiology and Immunology, Vanderbilt
                    University, A5119 MCN, Nashville, Tennessee 37232-2363,
                    USA.. james.tam@vanderbilt.edu
CONTRACT NUMBER:    AI46164 (NIAID)
SOURCE:             JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Dec 27) 277 (52)
                    50450-6.
                    Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200302
ENTRY DATE:         Entered STN: 20021227
                    Last Updated on STN: 20030228
                    Entered Medline: 20030227
AB   The electrostatic interaction of the charge cluster of an amphipathic
       ***peptide***     ***antibiotic***   with microbial membranes is a
     salt-sensitive step that often determines organism specificity.  We have
     examined the correlation between charge clusters and salt insensitivity
     and microbial specificity in linear, cyclic, and retro-isomeric
     cystine-stabilized   ***beta***  -  ***strand***   (CSbeta) tachyplesin
     (TP) in a panel of 10 test organisms.  Cyclic tachyplesins consisting of
     14 and 18 amino acids are constrained by an end-to-end   ***peptide***
     backbone and two or three disulfide bonds to cross-brace the anti-parallel
       ***beta***  -  ***strand***   that approximates a "beta-tile" structure.
     Circular dichroism measurements of beta-tile TPs showed that they
     displayed ordered structures.  Control   ***peptides***   containing the
     same number of basic amino acids as TP but lacking disulfide constraints
     were highly salt sensitive.  Cyclic TP analogues with six cationic charges
     were more broadly active and salt-insensitive than those with fewer
     cationic charges.  Reducing their proximity or number of cationic charges,
     particularly those with three or fewer basic amino acids, led to a
     significant decrease in potency and salt insensitivity, but an increased
     selectivity to certain Gram-positive bacteria.  An end-group effect of the
     dibasic N-terminal Lys of TP in the open-chain TP and its retroisomer was
     observed in certain Gram-negative bacteria under high-salt conditions, an
     effect that was not found in the cyclic analogs.  These results suggest
     that a stable folded structure together with three or more basic amino
     acids closely packed in a charged region in CSbeta   ***peptides***   is
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important for salt insensitivity and organism specificity.

L7 ANSWER 2 OF 11 MEDLINE
ACCESSION NUMBER: 2001435766 MEDLINE
DOCUMENT NUMBER: 21240126 PubMed ID: 11341843
TITLE: Design of Gram-negative selective antimicrobial peptides.
AUTHOR: Muhle S A; Tam J P
CORPORATE SOURCE: Department of Microbiology and Immunology, Vanderbilt University, A5119 MCN, Nashville, Tennessee 37232, USA.
CONTRACT NUMBER: 5T32CA09582 (NCI)
5T32GM07347 (NIGMS)
CA36544 (NCI)
SOURCE: BIOCHEMISTRY, (2001 May 15) 40 (19) 5777-85.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010806
Last Updated on STN: 20010806
Entered Medline: 20010802

AB Lipopolysaccharide (LPS), a major component of Gram-negative bacteria, signals bacterial invasion and triggers defensive host responses. However, excessive responses also lead to the serious pathophysiological consequence of septic shock. To develop Gram-negative selective compounds that can inhibit the effects of LPS-induced sepsis, we have designed constrained cyclic antimicrobial ***peptides*** based on a cystine-stabilized ***beta*** - ***stranded*** framework mimicking the putative LPS-binding sites of the LPS-binding protein family. Our prototype termed R4A, c(PACRCRAG-PARCRCAG), consists of an eight amino acid degenerated repeat constrained by a head-to-tail cyclic ***peptide*** backbone and two cross-bracing disulfides. NMR study of K4A, an R4A analogue with four Arg --> Lys replacements, confirmed the amphipathic design elements with four Lys on one face of the antiparallel ***beta*** - ***strand*** and two hydrophobic cystine pairs plus two Ala on the opposite face. K4A and R4A displayed moderate microbicidal potency and Gram-negative selectivity. However, R4A analogues with single or multiple replacements of Ala and Gly with Arg or bulky hydrophobic amino acids displayed increased potency and selectivity in both low- and high-salt conditions. Analogues R5L and R6Y containing additional cationic and bulky hydrophobic amino acids proved the best mimics of the amphipathic topology of the "active-site" ***beta*** - ***strands*** of LPS-binding proteins. They displayed potent activity against Gram-negative E. coli with a minimal inhibitory concentration of 20 nM and a >200-fold selectivity over Gram-positive S. aureus. Our results suggest that an LPS-targeted design may present an effective approach for preparing selective ***peptide*** ***antibiotics*** .

L7 ANSWER 3 OF 11 MEDLINE
ACCESSION NUMBER: 2000149916 MEDLINE
DOCUMENT NUMBER: 20149916 PubMed ID: 10685049
TITLE: Synthesis, microbicidal activity, and solution structure of the dodecapeptide from bovine neutrophils.
AUTHOR: Raj P A; Karunakaran T; Sukumaran D K
CORPORATE SOURCE: School of Dentistry, Marquette University, Milwaukee, WI, USA.. Periathambya@vms.csd.mu.edu
CONTRACT NUMBER: DE04898 (NIDCR)
SOURCE: BIOPOLYMERS, (2000 Apr 5) 53 (4) 281-92.
Journal code: 0372525. ISSN: 0006-3525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000413
Last Updated on STN: 20000413
Entered Medline: 20000331

AB The dodecapepetide sequence R-L-C-R-I-V-V-I-R-V-C-R with a disulfide bridge between the cysteine residues found in bovine neutrophils was synthesized by solid-phase procedures. Its antimicrobial activity against oral microorganisms such as Actinobacillus actinomycetemcomitans,

Porphyromonas gingivalis, Streptococcus mutans, and Streptococcus gordonii was examined, and its structural features were examined by CD and determined by two-dimensional (2D) nmr. The strains P. gingivalis (W50 and 381), A. actinomycetemcomitans (Y4 and 67), S. gordonii (DL1), and S. mutans (GS5) are found to be highly sensitive to this ***peptide*** at 2-2.5 microM concentrations, suggesting that the dodecapeptide is a potent ***antibiotic*** for oral pathogens. The weak negative n-sigma* band observed at approximately 265-270 nm in the CD spectra of this ***peptide*** provides evidence for the presence of a disulfide bridge. The negative n-pi* band at approximately 200 nm and the positive pi-pi* band at 185 nm suggest a folded structure for this ***peptide*** . The negative n-pi* shifts from 200 to 206 nm with an increase in intensity in dipalmitoylphosphotidylcholine vesicles, suggesting that the ***peptide*** might associate to form higher order aggregates in lipid medium. The assignment of backbone and side-chain proton resonances has been accomplished by the combined analysis of 2D total correlated and nuclear Overhauser effect spectroscopy. The temperature dependence of amide NH chemical shifts and (1)H-(2)H exchange effect on amide NH resonances indicate the involvement of amide NH groups of Cys3, Ile5, Ile8, Val10, and Arg12 in intramolecular hydrogen bonding. The coupling constant (J(NH-C(alpha)H)) values, the set of medium-, short-, and long-range nuclear Overhauser effects, and the results of restrained structure calculation using the distance geometry algorithm for nmr applications provide evidence for a folded, loop-like structure with a type I (III) beta-turn involving Ile5, Val6, Val7, and Ile8, and two antiparallel ***beta*** - ***strands*** involving the N-terminal Arg1, Leu2, Cys3, and Val4 and the C-terminal Arg9, Val10, Cys11, and Arg12 residues. The structure of the dodecapeptide mimics the amphiphilic structure of large 30-35 residue defensins and the ***peptide*** appears to exhibit similar antimicrobial potency.

L7 ANSWER 4 OF 11 MEDLINE
ACCESSION NUMBER: 2000139728 MEDLINE
DOCUMENT NUMBER: 20139728 PubMed ID: 10673369
TITLE: Marked increase in membranolytic selectivity of novel cyclic tachyplesins constrained with an antiparallel two-beta strand cystine knot framework.
AUTHOR: Tam J P; Lu Y A; Yang J L
CORPORATE SOURCE: Department of Microbiology, Vanderbilt University, MCN A5119, Nashville, Tennessee, 37232-2363, USA.. james.tam@mcmail.vanderbilt.edu
CONTRACT NUMBER: AI46164 (NIAID)
CA36544 (NCI)
GM57145 (NIGMS)
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2000 Jan 27) 267 (3) 783-90.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000320
Last Updated on STN: 20000320
Entered Medline: 20000309

AB We have developed a highly constrained 18-residue cyclic ***peptide*** template based on the antimicrobial ***peptide*** tachyplesin-1 that features an end-to-end ***peptide*** backbone and a cystine knot-like motif with three evenly spaced disulfide bonds to cross-brace the antiparallel ***beta*** - ***strands*** and to approximate an amphiphatic "beta-tile"-like structure. Six beta-tile analogs were prepared to correlate different topological patterns with membranolytic specificity. Their conformations and antimicrobial and hemolytic activities were compared with tachyplesin-1 and the recently discovered Rhesus monkey theta defensin (RTD) which contains similar beta-tile structural elements. The beta-tile ***peptides*** and RTD retained broad spectrum antimicrobial activities. In general, they were less active than tachyplesin-1 in 10 tested organisms but their activity increased under high-salt (100 mM NaCl) rather than in low-salt conditions. The beta-tile ***peptides*** are highly nontoxic to human erythrocytes with EC(25) ranging from 600 to 4000 microM. Collectively,

our results show that the design of a highly rigid ***peptide*** template is useful for further analog study to dissociate antimicrobial activity from cytotoxicity which would be helpful in discovering clinical applications for ***peptide*** ***antibiotics*** .

L7 ANSWER 5 OF 11 MEDLINE
ACCESSION NUMBER: 95191538 MEDLINE
DOCUMENT NUMBER: 95191538 PubMed ID: 7885338
TITLE: [Design of de novo specific DNA-binding peptides, using the motif beta-chain-turn-beta-chain for recognizing a nucleotide sequence in DNA].
Konstruirovanie de novo spetsifichnykh DNK-sviazyvaiushchikh peptidov, ispol'zuiushchikh motiv beta-tsep'-povorot-beta-tsep' dlia uznavaniia nukleotidnoi posledovatel'nosti na DNK.
AUTHOR: Surovaia A N; Grokhovskii S L; Brusov R V; Lysov Iu P; Zhuze A L; Gurskii G V
SOURCE: MOLEKULIARNAIA BIOLOGIIA, (1994 Nov-Dec) 28 (6) 1383-99.
Journal code: 0105454. ISSN: 0026-8984.
PUB. COUNTRY: RUSSIA: Russian Federation
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 19950425
Last Updated on STN: 19950425
Entered Medline: 19950407
AB De novo design and synthesis by a solid phase technique of linear and cyclic 26-residues ***peptides*** are reported. The ***peptides*** use ***beta*** - ***strand*** -turn- ***beta*** - ***strand*** motif for sequence recognition on DNA. Amino acid sequences in the two ***peptides*** are identical, but the structure of the cyclic ***peptide*** is constrained by S-S bridge between two cysteine residues. A 28-residue ***peptide*** containing at the N-terminus a copper-chelating ***peptide*** Gly-Gly-His is also synthesized which can be used as a potential DNA-cleaving reagent. Binding of these ***peptides*** to various natural and synthetic DNAs and DNA fragment with a known base pair sequence has been studied by CD spectroscopy, fluorescence methods and DNAse I footprinting technique. By means of CD spectroscopy it is shown that 26-residue linear and cyclic ***peptides*** are partially in disordered and beta-conformations in aqueous solution in absence and in presence of 20% trifluoroethanol (TFE), but assume partially an alpha-helix conformation in the presence of 50% TFE. It is shown that linear and cyclic ***peptides*** bind to DNA. The binding approaches saturation level when one ***peptide*** molecule is bound approximately per three or four DNA base pairs. We found that ***antibiotic*** distamycin A, binding in the minor DNA groove, competes effectively with the 26-residue linear and cyclic ***peptides*** for binding to poly(dA).poly (dT). According to the CD spectroscopy data the linear and cyclic ***peptides*** undergo conformation changes upon binding to DNA, whereas the DNA structure is not markedly altered. Difference CD spectra obtained by subtracting the spectrum of the free DNA from the spectrum of the ***peptide*** -DNA mixture differ from the spectrum of the free ***peptide*** . The shapes of difference CD spectra are consistent with a conformation transition from a disordered conformation into a beta-like conformation upon binding of ***peptide*** to DNA. DNAase I footprinting diagrams show that there is a specific protection by linear and cyclic ***peptides*** of the nucleotide sequences on two ends of operators OR1, OR2 and OR3 and pseudooperators within the cro gene of 434 phage.

L7 ANSWER 6 OF 11 MEDLINE
ACCESSION NUMBER: 90064490 MEDLINE
DOCUMENT NUMBER: 90064490 PubMed ID: 2585485
TITLE: Crystallographic mapping of beta-lactams bound to a D-alanyl-D-alanine peptidase target enzyme.
AUTHOR: Kelly J A; Knox J R; Zhao H; Frere J M; Ghaysen J M
CORPORATE SOURCE: Department of Molecular and Cell Biology, University of Connecticut, Storrs 06269.
CONTRACT NUMBER: GM37742 (NIGMS)
RR01955 (NCRR)

SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (1989 Sep 20) 209 (2) 281-95.
Journal code: 985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199001
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 20000303
Entered Medline: 19900103

AB X-ray crystallography has been used to examine the binding of three members of the beta-lactam family of ***antibiotics*** to the D-alanyl-D-alanine peptidase from Streptomyces R61, a target of penicillins. Cephalosporin C, the monobactam analog of penicillin G and (2,3)-alpha-methylene benzylpenicillin have been mapped at 2.3 A resolution in the form of acyl-enzyme complexes bound to serine 62. On the basis of the positions of these inhibitors, the binding of a tripeptide substrate for the enzyme, L-lysyl-D-alanyl-D-alanine, has been modeled in the active site. The binding of both inhibitors and substrate is facilitated by hydrogen-bonding interactions with a conserved ***beta*** - ***strand*** (297-303), which is antiparallel to the beta-lactam's acylamide linkage or the substrate's ***peptide*** bond. The active site is similar to that in beta-lactamases.

L7 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:93817 CAPLUS
DOCUMENT NUMBER: 134:292431
TITLE: Cyclic cystine-knot .beta.-stranded antimicrobial peptides: Occurrence, design and synthesis
AUTHOR(S): Tam, James P.; Lu, Yi-An; Yang, Jin-Long; Yu, Qitao
CORPORATE SOURCE: Dept. Microbiol. Immunol., Vanderbilt University, Nashville, TN, 37232-2363, USA
SOURCE: Development of Novel Antimicrobial Agents: Emerging Strategies (2001), 215-240. Editor(s): Lohner, Karl. Horizon Scientific Press: Wymondham, UK.
CODEN: 69AXXR
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English

AB A review contg. 73 refs. Amphipathicity of antimicrobial ***peptides*** is an important attribute to their membranolytic actions. However, the relationship of amphipathicity to membranolytic selectivity that dissocs. cytotoxicity from antimicrobial activity remains poorly understood. Analog study using rigid preorganized amphipathic structures may provide insight for selective interactions with microbial rather than eukaryotic membrane. Cyclic cystine-knot ***peptides*** with two or three . ***beta*** . ***strands*** , referred as cc3.beta.2 and cc3.beta.3 ***peptides*** resp., represent novel and highly constrained scaffoldings of antimicrobial ***peptides*** contg. 18 to 33 amino acid residues. This report describes their natural occurrence in higher organisms as well as our efforts in designing and developing new synthetic methods for cc3.beta.2, cc3.beta.3 ***peptides*** and their analogs. The rigidity imparted by the close-ended amide backbone and the tricystine constraints of cc3.beta.2 and cc3.beta.3 ***peptides*** also facilitates developing therapeutic useful ***peptide*** ***antibiotics*** of . ***beta*** .- ***stranded*** defensins, tachyplesins and protegrins that are membrane-selective, salt-insensitive and low cytotoxicity.

REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:559741 CAPLUS
DOCUMENT NUMBER: 115:159741
TITLE: Structure elucidation and solution conformation of the glycopeptide antibiotic ramoplanose (UK-71,903): a cyclic depsipeptide containing an antiparallel .beta.-sheet and a .beta.-bulge
AUTHOR(S): Skelton, Nicholas J.; Harding, Margaret M.; Mortishire-Smith, Russell J.; Rahman, Shirley K.; Williams, Dudley H.; Rance, Michael J.; Ruddock, John C.
CORPORATE SOURCE: Univ. Chem. Lab., Cambridge Cent. Mol. Recognit.,

SOURCE: Cambridge CB2 1EW, UK
Journal of the American Chemical Society (1991), 113(20), 7522-30
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The primary structure of ramoplanose (UK-71,903), a new member of the group of ***antibiotics*** related to ramoplanin A2, has been detd. by a combination of chem. and spectroscopic methods. Ramoplanose differs from ramoplanin A2 in having a branched chain mannose-contg. trisaccharide and a cis-trans N-terminal dienic fatty acid. The dominant soln. conformation of the ***antibiotic*** aglycon was detd. by using distance geometry and restrained mol. dynamics calcns. Input for these calcns. was provided by 97 interresidue distance constraints obtained from nuclear Overhauser enhancement spectroscopy. Each of the resulting family of five structures contains two antiparallel . ***beta*** .- ***strands*** connected by seven intramol. hydrogen bonds and two reverse turns. One strand also incorporates a .beta.-bulge. The stereochemistries of the amino acids along the ***peptide*** backbone induce curvature in the .beta.-sheet, and a cleft is formed that may represent the active site.

L7 ANSWER 9 OF 11 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:520235 BIOSIS
DOCUMENT NUMBER: PREV199396133642
TITLE: Solution structures of the lantibiotics duramycin B and C.
AUTHOR(S): Zimmerman, Norbert; Freund, Stefan; Fredenhagen, Andreas; Jung, Guenther (1)
CORPORATE SOURCE: (1) Institut fuer Organische Chemie, Eberhard-Karls-Universitaet Tuebingen, Auf der Morgenstelle 18, D-72076 Tuebingen Germany
SOURCE: European Journal of Biochemistry, (1993) Vol. 216, No. 2, pp. 419-428.
ISSN: 0014-2956.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The solution structures of the lantibiotics duramycin B in H-2O/2H-2O (9:1) and duramycin C in (2H-3)acetonitrile/H-2O (1:1) have been determined by NMR followed by distance-geometry and restrained-molecular-mechanics calculations. The constitution and location of three thioether bridges and a lysinoalanine ring system could be established by unambiguously assigned NOE contacts between the bridging side chains. Model building based on NMR constraints resulted in a U-shaped topology of the tetracyclic 19- ***peptides*** with a turn around Pro9 and a kink along a virtual line from residues 5 to 13. This clamp-like conformation is stabilized by the thioether brides and is additionally supported by an antiparallel ***beta*** - ***strand*** -like structure of the N-termini and C-termini and the inherent amphiphilicity of duramycin-type ***antibiotics*** . The duramycins B and C differ mainly in the relative mobilities of their rings A, C and D. Duramycin B is closely related to cinnamycin with an exchange of Phe10 to leucine, whereas duramycin C differs from duramycin B by three conserved and two non-conserved amino-acid exchanges.

L7 ANSWER 10 OF 11 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 82228611 EMBASE
DOCUMENT NUMBER: 1982228611
TITLE: Structure of a Zn2+-containing D-alanyl-D-alanine-cleaving carboxypeptidase at 2.5 .ANG. resolution.
AUTHOR: Dideberg O.; Charlier P.; Dive G.; et al.
CORPORATE SOURCE: Lab. Cristallogr., Inst. Phys., Univ. Liege, B-4000 Sart Tilman, Liege, Belgium
SOURCE: Nature, (1982) 299/5882 (469-470).
CODEN: NATUAS
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 004 Microbiology
LANGUAGE: English

AB Bacteria possess proteases that are specific for the ***peptide*** bonds between D-alanine residues, one of which has a free .alpha.-carboxyl group. These D-alanyl-D-alanine peptidases catalyse carboxypeptidation and transpeptidation reactions involved in bacterial cell wall metabolism, and

are inactivated by .beta.-lactam ***antibiotics*** . We have now elucidated the structure, at 2.5 .ANG. resolution, of the penicillin-resistant Zn2+-containing D-alanyl-D-alanine peptidase of Streptomyces albus (Zn2+ G peptidase). The enzyme is shown to consist of two globular domains, connected by a single link. The N-terminal domain has three .alpha.-helices, and the C-terminal domain has three .alpha.-helices and five . ***beta*** .- ***strands*** . The Zn2+ ion is ligated by three histidine residues, and located in a cleft in the C-terminal domain. The mechanism of action of the enzyme may be related to that of other carboxypeptidases, which also contain functional Zn2+ ions.

L7 ANSWER 11 OF 11 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 95:248446 SCISEARCH
THE GENUINE ARTICLE: QQ024
TITLE: DESIGN OF DE-NOVO DNA-BINDING PEPTIDES WITH THE BETA-STRAND-TURN-BETA-STRAND MOTIF FOR DNA-SEQUENCE RECOGNITION
AUTHOR: SUROVAYA A N (Reprint); GROKHOVSKII S L; BRUSOV R V; LYSOV Y P; ZHUZE A L; GURSKII G V
CORPORATE SOURCE: RUSSIAN ACAD SCI, VA ENGELHARDT MOLEC BIOL INST, MOSCOW 117984, RUSSIA (Reprint)
COUNTRY OF AUTHOR: RUSSIA
SOURCE: MOLECULAR BIOLOGY, (NOV/DEC 1994) Vol. 28, No. 6, Part 2, pp. 859-868.
ISSN: 0026-8933.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 49

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Hereby we report the design and solid-phase synthesis of de novo 26-residue linear and cyclic ***peptides*** with the ***beta*** - ***strand*** -turn- ***beta*** - ***strand*** motif for DNA sequence recognition; the only difference was the cyclic counterpart being conformationally restricted by a sulfhydryl bridge. Another product was a 28-residue ***peptide*** with N-terminal copper-chelating Gly-Gly-His, a potential DNA-cleaving agent. Binding of these ***peptides*** to natural DNAs, an endonuclease restriction fragment, and synthetic polydeoxyribonucleotides was examined by CD spectroscopy, fluorescence assays, and DNase I footprinting. The CD data showed the 26-residue linear and cyclic ***peptides*** to be in largely random and partly beta-conformation in water-or 20% trifluroethanol, but to assume a partly alpha-helical conformation in 50% TFE. Both the linear and the cyclic ***peptides*** were shown to bind to DNA, with saturation at one ***peptide*** per 3-4 bp. The ***antibiotic*** distamycin A, binding at the DNA minor groove, was found to compete with the ***peptides*** for the binding sites on poly(dA). poly(dT). The CD analysis revealed conformational alterations in the ***peptides*** upon binding to DNA, while the DNA structure underwent no appreciable changes. The CD difference spectra of the DNA- ***peptide*** mixture minus free DNA were distinct from those of the free ***peptide*** , and their shape was consistent with the random-to-beta-like conformational transition in the ***peptides*** upon binding to DNA. The DNase footprints showed that the linear and cyclic ***peptides*** specifically protected nucleotide sequences at the periphery of operators O(R)1, O(R)2, O(R)3 and pseudooperators in the phage 434 cro gene.

=> d his

(FILE 'HOME' ENTERED AT 10:08:38 ON 29 MAY 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 10:08:59 ON 29 MAY 2003

```
L1          4249 S ANTIBIOTIC PEPTIDE
L2         13485 S BETA-STRAND?
L3         13485 S BETA STRAND?
L4             1 S L1 (P) L2
L5            33 S PEPTIDE (P) ANTIBIOTIC (P) L2
L6            12 DUPLICATE REMOVE L5 (21 DUPLICATES REMOVED)
L7            11 S L6 NOT L4
```

```
=> s defensin or protrgrin or tachyplesin
L8        6969 DEFENSIN OR PROTRGRIN OR TACHYPLESIN

=> s disulfide bond
L9       45910 DISULFIDE BOND

=> s (l7 or l8) (p) l9
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L50) (P) L57'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L51) (P) L58'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L52) (P) L59'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L53) (P) L60'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L54) (P) L61'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L55) (P) L62'
L10        272 (L7 OR L8) (P) L9

=> s l10 (p) (no or devoid)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L64 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L65 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L66 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L67 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L68 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L69 (P) '
L11         48 L10 (P) (NO OR DEVOID)

=> d his

     (FILE 'HOME' ENTERED AT 10:08:38 ON 29 MAY 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     10:08:59 ON 29 MAY 2003
L1          4249 S ANTIBIOTIC PEPTIDE
L2         13485 S BETA-STRAND?
L3         13485 S BETA STRAND?
L4             1 S L1 (P) L2
L5            33 S PEPTIDE (P) ANTIBIOTIC (P) L2
L6            12 DUPLICATE REMOVE L5 (21 DUPLICATES REMOVED)
L7            11 S L6 NOT L4
L8          6969 S DEFENSIN OR PROTRGRIN OR TACHYPLESIN
L9         45910 S DISULFIDE BOND
L10          272 S (L7 OR L8) (P) L9
L11           48 S L10 (P) (NO OR DEVOID)

=> s vector? or target?
L12    1850814 VECTOR? OR TARGET?

=> s l10 (p) l12
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L64 (P) L78'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L65 (P) L79'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L66 (P) L80'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L67 (P) L81'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L68 (P) L82'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L69 (P) L83'
L13         20 L10 (P) L12
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=> duplicate remove l13
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L13
L14          10 DUPLICATE REMOVE L13 (10 DUPLICATES REMOVED)

=> d his

     (FILE 'HOME' ENTERED AT 10:08:38 ON 29 MAY 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     10:08:59 ON 29 MAY 2003
L1         4249 S ANTIBIOTIC PEPTIDE
L2        13485 S BETA-STRAND?
L3        13485 S BETA STRAND?
L4            1 S L1 (P) L2
L5           33 S PEPTIDE (P) ANTIBIOTIC (P) L2
L6           12 DUPLICATE REMOVE L5 (21 DUPLICATES REMOVED)
L7           11 S L6 NOT L4
L8         6969 S DEFENSIN OR PROTRGRIN OR TACHYPLESIN
L9        45910 S DISULFIDE BOND
L10         272 S (L7 OR L8) (P) L9
L11          48 S L10 (P) (NO OR DEVOID)
L12     1850814 S VECTOR? OR TARGET?
L13          20 S L10 (P) L12
L14          10 DUPLICATE REMOVE L13 (10 DUPLICATES REMOVED)

=> s l14 not l6
L15          10 L14 NOT L6

=> d l15 1-10 ibib abs

L15  ANSWER 1 OF 10     MEDLINE
ACCESSION NUMBER:   2001679486     MEDLINE
DOCUMENT NUMBER:    21582858   PubMed ID: 11725546
TITLE:              Development of selective antagonists against an HIV second
                    receptor.
AUTHOR:             Tamamura H
CORPORATE SOURCE:   Graduate School of Pharmaceutical Sciences, Kyoto
                    University, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan.
SOURCE:             YAKUGAKU ZASSHI. JOURNAL OF THE PHARMACEUTICAL SOCIETY OF
                    JAPAN, (2001 Nov) 121 (11) 781-92.  Ref: 45
                    Journal code: 0413613. ISSN: 0031-6903.
PUB. COUNTRY:       Japan
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
                    (REVIEW, TUTORIAL)
LANGUAGE:           Japanese
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200201
ENTRY DATE:         Entered STN: 20011203
                    Last Updated on STN: 20020124
                    Entered Medline: 20020102
AB   The authors have discovered a highly selective CXCR4 antagonist, T22
     ([Tyr5,12, Lys7]-polyphemusin II), and its shortened potent analogs, T140
     and TC14012, which strongly inhibit the T-cell line-tropic HIV-1
     (X4-HIV-1) infection through their specific binding to a chemokine
     receptor, CXCR4.  CXCR4 is a major coreceptor (second receptor) for the
     entry of X4-HIV-1 into T-cells.  These peptides have been found through
     the structure-activity relationship (SAR) study on  ***tachyplesins***
     and polyphemusins, which function as self-defense peptides of horseshoe
     crabs with immature immune systems.  T140 and TC14012 showed the highest
     level of anti-HIV activity and antagonism of  ***target***  cell entry
     by X4-HIV-1 among all the CXCR4 antagonists that have been reported to
     date.  Additionally, bifunctional anti-HIV agents based on the specific
     CXCR4 antagonists (T140 analogs)-3'-azido-3'-deoxythymidine (AZT)
     conjugation have been synthesized and evaluated, since T140 analogs can
     possibly work as a carrier of AZT  ***targeting***  T-cells due to their
     specific affinity for CXCR4 on T-cells.  T22 have two  ***disulfide***
       ***bonds***  and a Trp residue in the molecule.  In connection with this
     study, novel facile and side-reaction-free methodologies for
       ***disulfide***  ***bond***  formation have been established for the
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increase of the efficiency of SAR studies. Furthermore, the completely stereocontrolled synthetic [redacted]cess for a couple of (E)-alken[redacted]ipeptide isosteres starting from L-amino acid has been established in order to facilitate nonpeptidylation studies on peptide-lead candidates. In this review, the authors wish to summarize our recent research on the development of specific antagonists against the HIV second receptor CXCR4, involving studies on the establishment of efficient methodologies for the facile synthesis of peptides and peptide mimetics.

L15 ANSWER 2 OF 10 MEDLINE
ACCESSION NUMBER: 94212353 MEDLINE
DOCUMENT NUMBER: 94212353 PubMed ID: 7512758
TITLE: ***Defensins*** : a family of antimicrobial and cytotoxic peptides.
AUTHOR: Kagan B L; Ganz T; Lehrer R I
CORPORATE SOURCE: Department of Psychiatry and Biobehavioral Science, BRI UCLA-Center for Health Sciences.
CONTRACT NUMBER: AI 22839 (NIAID)
AI 29595 (NIAID)
MH 43433 (NIMH)
+
SOURCE: TOXICOLOGY, (1994 Feb 28) 87 (1-3) 131-49. Ref: 65
Journal code: 0361055. ISSN: 0300-483X.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940526
Last Updated on STN: 19960129
Entered Medline: 19940519
AB ***Defensins*** are antimicrobial and cytotoxic peptides that contain 29-35 amino acid residues, including 6 invariant cysteines that form 3 intramolecular ***disulfide*** ***bonds*** . They constitute more than 5% of the total cellular protein of human and rabbit neutrophils (PMN), and are also produced by rabbit lung macrophages and by murine and human small intestinal Paneth cells. ***Defensins*** exerted antimicrobial effects in vitro against many Gram-positive and Gram-negative bacteria, fungi, mycobacteria and some enveloped viruses, and were cytotoxic to a wide range of normal and malignant ***targets*** , including cells resistant to TNF-alpha and NK-cytolytic factor. Human and rabbit ***defensins*** formed voltage-sensitive channels in a variety of planar lipid bilayers when a negative voltage of approximately 70-90 mV was applied to the contralateral side. These channels showed modest anion selectivity and their formation was strongly influenced by ***defensin*** concentration. Although most other channel-forming peptides have prominent alpha-helical domains, the structure of ***defensin*** molecules is primarily composed of antiparallel beta-sheets. Studies with various prokaryotic and eukaryotic cells provided convincing evidence that ***defensins*** killed these ***targets*** by forming voltage-regulated channels in the susceptible cell's membrane. The broad spectrum of ***defensin*** -susceptible ***targets*** and the abundance of ***defensins*** in specialized host defense cells of the blood, lungs and intestinal tract suggest that ***defensins*** could play a significant role in innate immunity to infection and neoplasia.

L15 ANSWER 3 OF 10 MEDLINE
ACCESSION NUMBER: 93236814 MEDLINE
DOCUMENT NUMBER: 93236814 PubMed ID: 8476558
TITLE: ***Defensins*** : antimicrobial and cytotoxic peptides of mammalian cells.
AUTHOR: Lehrer R I; Lichtenstein A K; Ganz T
CORPORATE SOURCE: Department of Medicine, University of California, Los Angeles 90024.
CONTRACT NUMBER: AI 22839 (NIAID)
AI 29595 (NIAID)
HL 35640 (NHLBI)
SOURCE: ANNUAL REVIEW OF IMMUNOLOGY, (1993) 11 105-28. Ref: 101
Journal code: 8309206. ISSN: 0732-0582.

PUB. COUNTRY: United State[redacted]
DOCUMENT TYPE: Journal; Art[redacted]e; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-L08744; GENBANK-L08745; GENBANK-L08746; GENBANK-L08747; GENBANK-L08748; GENBANK-L12690; GENBANK-L12691; GENBANK-L23486; GENBANK-L23487; GENBANK-L23488
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 19930611
Last Updated on STN: 19950206
Entered Medline: 19930527

AB ***Defensins*** are antimicrobial and cytotoxic peptides that contain 29-35 amino acid residues, including six invariant cysteines whose intramolecular ***disulfide*** ***bonds*** cyclize and stabilize them in a complexly folded, triple-stranded beta-sheet configuration. Generated by the proteolytic processing of 93-95 amino acid precursor peptides, the constitute > 5% of the total cellular protein in human and rabbit neutrophils (polymorphonucleated neutrophils--PMN) and are also produced by rabbit lung macrophages and by mouse and rabbit small intestinal Paneth cells. Despite their prominence in rat PMN, ***defensins*** are not found in murine PMN. The antimicrobial spectrum of ***defensins*** includes gram positive and gram negative bacteria, mycobacteria, T. pallidum, many fungi, and some enveloped viruses. ***Defensins*** exert nonspecific cytotoxic activity against a wide range of normal and malignant ***targets*** , including cells resistant to TNF-alpha and NK-cytolytic factor. They appear to kill mammalian ***target*** cells and microorganisms by a common mechanism, which involves initial electrostatic interactions with negatively charged ***target*** cell surface molecules (likely the head groups of polar membrane lipids), followed by insertion into the cell membranes which they permeabilize, forming voltage-regulated channels. In addition to their antimicrobial and cytotoxic properties, some ***defensins*** act as opsonins, while others inhibit protein kinase C, bind specifically to the ACTH receptor and block steroidogenesis or act as selective chemoattractants for monocytes. ***Defensins*** are a newly delineated family of effector molecules whose contribution to host defense, inflammation, and cytotoxicity may be considerable for humans, even though it is unlikely to be revealed by experimentation with mice.

L15 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:335112 CAPLUS
DOCUMENT NUMBER: 135:92843
TITLE: Synthetic peptides derived from the .beta.2-.beta.3 loop of Raphanus sativus antifungal protein 2 that mimic the active site
AUTHOR(S): Schaaper, W. M. M.; Posthuma, G. A.; Plasman, H. H.; Sijtsma, L.; Fant, F.; Borremans, F. A. M.; Thevissen, K.; Broekaert, W. F.; Meloen, R. H.; Van Amerongen, A.
CORPORATE SOURCE: Institute for Animal Science and Health (ID-Lelystad), Lelystad, NL-8200 AB, Neth.
SOURCE: Journal of Peptide Research (2001), 57(5), 409-418
CODEN: JPERFA; ISSN: 1397-002X
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Rs-AFPs are antifungal proteins, isolated from radish (Raphanus sativus) seed or leaves, which consist of 50 or 51 amino acids and belong to the plant ***defensin*** family of proteins. Four highly homologous Rs-AFPs have been isolated (Rs-AFP1-4). The structure of Rs-AFP1 consists of three .beta.-strands and an .alpha.-helix, and is stabilized by four cystine bridges. Small peptides deduced from the native sequence, still having biol. activity, are not only important tools to study structure-function relationships, but may also constitute a com. interesting ***target*** . In an earlier study, the authors showed that the antifungal activity of Rs-AFP2 is concd. mainly in the .beta.2-.beta.3 loop. Here, the authors synthesized linear 19-mer peptides, spanning the entire .beta.2-.beta.3 loop, that were found to be almost as potent as Rs-AFP2. Cysteines, highly conserved in the native protein, are essential for maintaining the secondary structure of the

protein. Surprisingly, in [redacted] 19-mer loop peptides, cysteine can be replaced by .alpha.-aminobu[redacted]ic acid, which even improves t[redacted] antifungal potency of the peptides. Analogous cyclic 19-mer peptides, forced to adopt a hairpin structure by the introduction of one or two non-native disulfide bridges, were also found to possess high antifungal activity. The synthetic 19-mer peptides, like Rs-AFP2 itself, caused increased Ca2+ influx in pregerminated fungal hyphae.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:814517 CAPLUS
DOCUMENT NUMBER: 133:366399
TITLE: Antimicrobial theta- ***defensins*** and methods of using same
INVENTOR(S): Selsted, Michael E.; Tang, Yi-quan; Yuan, Jun; Ouellette, Andre J.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000068265	A1	20001116	WO 2000-US12842	20000510
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6335318	B1	20020101	US 1999-309487	19990510
EP 1187850	A1	20020320	EP 2000-930577	20000510
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6514727	B1	20030204	US 2001-967808	20010926

PRIORITY APPLN. INFO.: US 1999-309487 A2 19990510
WO 2000-US12842 W 20000510

OTHER SOURCE(S): MARPAT 133:366399

AB The present invention relates to an isolated cyclic peptide, .theta.- ***defensin*** , having antimicrobial activity, and to .theta.- ***defensin*** analogs. A .theta.- ***defensin*** can have the amino acid sequence Xaa1-Xaa2-Xaa3-Xaa4-Xaa5-Xaa1-Xaa6-Xaa4-Xaa4-Xaa1-Xaa1-Xaa6-Xaa4-Xaa5-Xaa1-Xaa3- aa7-Xaa8, wherein Xaa1 to Xaa8 are defined; wherein Xaa1 can be linked through a peptide bond to Xaa8; and wherein crosslinks can be formed between Xaa3 and Xaa3, between Xaa5 and Xaa5, and between Xaa7 and Xaa7. For example, the invention provides a .theta.- ***defensin*** having the amino acid sequence Gly-Phe-Cys-Arg-Cys-Leu-Cys-Arg-Arg-Gly-Val-Cys-Arg-Cys-Ile-Cys-Thr-Arg (SEQ ID NO:1), wherein the Gly at position 1 (Gly-1) is linked through a peptide bond to Arg-18, and wherein ***disulfide*** ***bonds*** are present between Cys-3 and Cys-16, between Cys-5 and Cys-14, and between Cys-7 and Cys-12. The invention also provides nucleic acids encoding .theta.- ***defensins*** and antibodies that specifically bind a .theta.- ***defensin*** . In addn., the invention relates to methods of using .theta.- ***defensin*** to reduce or inhibit microbial growth or survival.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:477649 CAPLUS
DOCUMENT NUMBER: 129:241281
TITLE: ***Defensins*** and related antibiotic peptides in evolution of defensive systems in animals
AUTHOR(S): Kokryakov, V. N.; Stefanov, V. E.; Alyoshina, G. M.;

Shamova, O. V.; Korneva, E. A.; Harwig, S.; Lehrer, R. I.
CORPORATE SOURCE: Institute of Experimental Medicine, Russian Academy of Medical Sciences, St. Petersburg, Russia
SOURCE: Journal of Evolutionary Biochemistry and Physiology (Translation of Zhurnal Evolyutsionnoi Biokhimii i Fiziologii) (1997), 33(1), 96-108
CODEN: JEBPA9; ISSN: 0022-0930
PUBLISHER: MAIK Nauka/Interperiodica Publishing
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with .apprx.120 refs. ***Defensins*** are antibacterial, antiviral, and cytotoxic peptides of cationic nature which were isolated (and then sequenced) from the mammalian and bird neutrophils, some types of macrophages, and Paneth cells. Representatives of this peptide class are characterized by a variable no. of the arginine and lysine residues as well as by the presence of six invariant cysteine residues forming intramol. ***disulfide*** ***bonds*** . ***Defensins*** are active substances towards Gram-pos. and Gram-neg. bacteria, many fungi, and some enveloped viruses. The most possible mechanism of antibiotic effect of ***defensins*** consists in perforation of the ***target*** cell membranes and alteration of their barrier and metabolic functions. ***Defensins*** are able to play a many-sided role in immune responses of the organism: from a direct inactivation of various microorganisms during phagocytosis to a modulation of endocrinoimmune interactions. ***Defensins*** are evolutionary ancient, physiol. active substances participating in formation of immune responses in the organism.
REFERENCE COUNT: 119 THERE ARE 119 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:446971 CAPLUS
DOCUMENT NUMBER: 119:46971
TITLE: ***Defensins*** : Endogenous antibiotic peptides from human leukocytes
AUTHOR(S): Lehrer, Robert I.; Ganzt, Tomas
CORPORATE SOURCE: Dep. Med., Univ. California, Los Angeles, CA, 90024, USA
SOURCE: Ciba Foundation Symposium (1992), 171(Secondary Metabolites: Their Function and Evolution), 276-93
CODEN: CIBSB4; ISSN: 0300-5208
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with 47 refs. A variety of endogenous antimicrobial peptides equip mammals, amphibians, insects and plants to defend themselves against microbial pathogens. ***Defensins*** are small peptides of mammalian cells that contain 29-35 amino acid residues, including six invariant cysteines that form three intramol. ***disulfide*** ***bonds*** . They are produced by the sequential proteolysis of precursors that contain approx. 95 amino acids and are synthesized by several types of cells, esp. the bone marrow precursors of blood neutrophils. In certain mammalian species lung macrophages and specialized epithelial (Paneth) cells in the small intestine also produce ***defensins*** . ***Defensins*** are complexly folded, amphipathic, rich in antiparallel .beta.-sheet but devoid of .alpha.-helical domains. Their unusually broad antimicrobial spectrum encompasses gram-pos. and gram-neg. bacteria, many fungi, myobacteria, spirochetes and several enveloped viruses. The antimicrobial properties of ***defensins*** result from their insertion into ***target*** cell membranes and the formation of voltage-sensitive channels.

L15 ANSWER 8 OF 10 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:166344 BIOSIS
DOCUMENT NUMBER: PREV199800166344
TITLE: ***Defensins*** and related antibiotic peptides in the evolution of animal defense systems.
AUTHOR(S): Kokryakov, V. N. (1); Stefanov, V. E.; Aleshina, G. M.; Shamova, O. V.; Korneva, E. A.; Harwig, S. S.; Lehrer, R. I.
CORPORATE SOURCE: (1) Res. Inst. Exp. Med., Russ. Acad. Med. Sci., St.

Petersburg Russia
SOURCE: Zhurnal Evol[redacted]sionnoi Biokhimii i Fiziologii [redacted]Jan.-Feb., 1997) Vol. 33, No. 1, pp. 109-123.
ISSN: 0044-4529.
DOCUMENT TYPE: General Review
LANGUAGE: Russian
SUMMARY LANGUAGE: Russian
AB ***Defensins*** are cationic antibacterial, antiviral, and cytotoxic peptides isolated and sequenced from mammalian and avian neutrophils, some macrophage types and Paneth's cells. The representatives of this group of peptides are characterized by the presence of a variable number of arginine and lysine residues as well as six invariant cysteine residues forming intramolecular ***disulfide*** ***bonds*** .
Defensins are active with respect to gram-positive and gram-negative bacteria, various fungi and some viruses. Membrane perforation of ***target*** cells and disturbance of their barrier and metabolic functions were found to be the most probable mechanisms of the antibiotic effect of ***defensins*** . ***Defensins*** can play diverse roles in defense responses of the body: from immediate inactivation of various microorganisms during phagocytosis to modulation of endocrine-immune interactions. ***Defensins*** are evolutionary ancient, physiologically active substances participating in the development of defense responses.

L15 ANSWER 9 OF 10 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97098321 EMBASE
DOCUMENT NUMBER: 1997098321
TITLE: Ribosomally synthesized antimicrobial peptides: Their function, structure, biogenesis, and mechanism of action.
AUTHOR: Nissen-Meyer J.; Nes I.F.
CORPORATE SOURCE: J. Nissen-Meyer, Department of Biochemistry, University of Oslo, Post 1401, Blindern, 0316, Norway
SOURCE: Archives of Microbiology, (1997) 167/2-3 (67-77).
Refs: 89
ISSN: 0302-8933 CODEN: AMICCW
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Ribosomally synthesized peptides with antimicrobial activity are produced by prokaryotes, plants, and a wide variety of animals, both vertebrates and invertebrates. These peptides represent an important defense against micro-organisms. Although the peptides differ greatly in primary structures, they are nearly all cationic and very often amphiphilic, which reflects the fact that many of these peptides kill their ***target*** cells by permeabilizing the cell membrane. Moreover, many of these peptides may roughly be placed into one of three groups: (1) those that have a high content of one (or two) amino acid(s), often proline, (2) those that contain intramolecular ***disulfide*** ***bonds*** , often stabilizing a predominantly .beta.-sheet structure, and (3) those with amphiphilic regions if they assume an .alpha.-helical structure. Most known ribosomally synthesized antimicrobial peptides have been identified and characterized during the past 15 years. As a result of these studies, insight has been gained into fundamental aspects of biology and biochemistry such as innate immunity, membrane-protein interactions, and protein modification and secretion. Moreover, it has become evident that these peptides may be developed into useful antimicrobial additives and drugs. This review presents a broad overview of the main types of ribosomally synthesized antimicrobial peptides produced by eukaryotes and prokaryotes.

L15 ANSWER 10 OF 10 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95326370 EMBASE
DOCUMENT NUMBER: 1995326370
TITLE: Peptides as weapons against microorganisms in the chemical defense system of vertebrates.
AUTHOR: Nicolas P.; Mor A.
CORPORATE SOURCE: Laboratoire Bioactivation Peptides, Institut Jacques Monod, Universite Paris, 7, 2 place Jussieu,75251 Paris Cedex 05, France
SOURCE: Annual Review of Microbiology, (1995) 49/- (277-304).

ISSN: 0066-4227 CODEN: ARMIAZ
COUNTRY: United State
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The innate immunity of vertebrates to microbial invasion is arbitrated by a network of host-defense mechanisms involving both the long-lasting highly specific responses of the cell-mediated immune system and a nonspecific chemical defense system based on a series of broad-spectrum antimicrobial peptides that are analogous to those found in insects. Vertebrate antibiotic cells (91) and secreted into the lumen, in a pattern similar to the Paneth cell secretion of lysozyme. Active secretion of intestinal ***defensins*** would distinguish them from phagocyte ***defensins*** , which are not normally secreted and are primarily ***targeted*** for intracellular delivery to phagolysosomes. These observations suggest two possible, nonexclusive physiological roles for enteric ***defensins*** (41). First, secretion of ***defensins*** into the space above the crypt may contribute to the establishment of a local antibacterial milieu that limits bacterial colonization and invasion of the small bowel. Second, the ***defensins*** could be important in mucosal defense against microbial invasion by preserving the integrity of the villus epithelium and thereby maintaining the critical function of nutrient absorption. The tracheal antimicrobial peptide (TAP) is a new member of the .beta.- ***defensin*** family, originally isolated from the bovine tracheal mucosa (23, 24). Like .beta.- ***defensins*** of neutrophils, TAP is a basic molecule with a broad-spectrum antimicrobial activity and contains six cysteines, all involved in ***disulfide*** ***bonds*** (Table 2). In situ hybridization of TAP mRNA indicated that TAP is expressed along the entire length of the conducting airways, from nasal to bronchiolar tissues. TAP mRNA is localized in columnar cells of the pseudostratified epithelium, suggesting its expression in the ciliated cells. The fact that the .beta.- ***defensins*** found in circulating phagocytes, and TAP from the tracheal epithelium, are members of the same family of antimicrobial peptides strongly supports the hypothesis that TAP contributes to the host defense of the airways.

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     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     10:08:59 ON 29 MAY 2003
L1          4249 S ANTIBIOTIC PEPTIDE
L2         13485 S BETA-STRAND?
L3         13485 S BETA STRAND?
L4             1 S L1 (P) L2
L5            33 S PEPTIDE (P) ANTIBIOTIC (P) L2
L6            12 DUPLICATE REMOVE L5 (21 DUPLICATES REMOVED)
L7            11 S L6 NOT L4
L8          6969 S DEFENSIN OR PROTRGRIN OR TACHYPLESIN
L9         45910 S DISULFIDE BOND
L10          272 S (L7 OR L8) (P) L9
L11           48 S L10 (P) (NO OR DEVOID)
L12      1850814 S VECTOR? OR TARGET?
L13           20 S L10 (P) L12
L14           10 DUPLICATE REMOVE L13 (10 DUPLICATES REMOVED)
L15           10 S L14 NOT L6

=> s signal  (w) (agent or peptide)
L16       41608 SIGNAL (W) (AGENT OR PEPTIDE)

=> s l16 and l15
L17           0 L16 AND L15

=> s l10 and 16
L18          15 L10 AND 16

=> s l18 and l12
L19           1 L18 AND L12
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L19 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:814517 CAPLUS
DOCUMENT NUMBER: 133:366399
TITLE: Antimicrobial theta- ***defensins*** and methods of using same
INVENTOR(S): Selsted, Michael E.; Tang, Yi-quan; Yuan, Jun; Ouellette, Andre J.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000068265	A1	20001116	WO 2000-US12842	20000510
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6335318	B1	20020101	US 1999-309487	19990510
EP 1187850	A1	20020320	EP 2000-930577	20000510
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6514727	B1	20030204	US 2001-967808	20010926

PRIORITY APPLN. INFO.: US 1999-309487 A2 19990510
WO 2000-US12842 W 20000510
OTHER SOURCE(S): MARPAT 133:366399
AB The present invention relates to an isolated cyclic peptide, .theta.- ***defensin*** , having antimicrobial activity, and to .theta.- ***defensin*** analogs. A .theta.- ***defensin*** can have the amino acid sequence Xaa1-Xaa2-Xaa3-Xaa4-Xaa5-Xaa1-Xaa6-Xaa4-Xaa4-Xaa1-Xaa1-Xaa6-Xaa4-Xaa5-Xaa1-Xaa3- aa7-Xaa8, wherein Xaa1 to Xaa8 are defined; wherein Xaa1 can be linked through a peptide bond to Xaa8; and wherein crosslinks can be formed between Xaa3 and Xaa3, between Xaa5 and Xaa5, and between Xaa7 and Xaa7. For example, the invention provides a .theta.- ***defensin*** having the amino acid sequence Gly-Phe-Cys-Arg-Cys-Leu-Cys-Arg-Arg-Gly-Val-Cys-Arg-Cys-Ile-Cys-Thr-Arg (SEQ ID NO:1), wherein the Gly at position 1 (Gly-1) is linked through a peptide bond to Arg-18, and wherein ***disulfide*** ***bonds*** are present between Cys-3 and Cys- ***16*** , between Cys-5 and Cys-14, and between Cys-7 and Cys-12. The invention also provides nucleic acids encoding .theta.- ***defensins*** and antibodies that specifically bind a .theta.- ***defensin*** . In addn., the invention relates to methods of using .theta.- ***defensin*** to reduce or inhibit microbial growth or survival.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 10:08:38 ON 29 MAY 2003)

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L11          48 S L10 (P) (NO OR DEVOID)
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L15          10 S L14 NOT L6
L16       41608 S SIGNAL  (W) (AGENT OR PEPTIDE)
L17           0 S L16 AND L15
L18          15 S L10 AND 16
L19           1 S L18 AND L12

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   87.87      88.08

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -5.21      -5.21

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